

Notice of Allowability	Application No. 09/308,080	Applicant(s) GONZALEZ ET AL.
	Examiner Delia M. Ramirez	Art Unit 1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1.  This communication is responsive to 12/15/2003.
2.  The allowed claim(s) is/are 1-6, 8-11 and 29-36.
3.  The drawings filed on 5/12/1999 are accepted by the Examiner.
4.  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a)  All
  - b)  Some\* c)  None of the:
    1.  Certified copies of the priority documents have been received.
    2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3.  Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\* Certified copies not received: \_\_\_\_\_.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

**THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.**

5.  A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
6.  CORRECTED DRAWINGS ( as "replacement sheets") must be submitted.
  - (a)  including changes required by the Notice of Draftsperson's Patent Drawing Review ( PTO-948) attached
    - 1)  hereto or 2)  to Paper No./Mail Date \_\_\_\_\_.
  - (b)  including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date \_\_\_\_\_.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
7.  DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

#### Attachment(s)

1.  Notice of References Cited (PTO-892)
2.  Notice of Draftsperson's Patent Drawing Review (PTO-948)
3.  Information Disclosure Statements (PTO-1449 or PTO/SB/08),  
Paper No./Mail Date 12/15/03
4.  Examiner's Comment Regarding Requirement for Deposit  
of Biological Material
5.  Notice of Informal Patent Application (PTO-152)
6.  Interview Summary (PTO-413),  
Paper No./Mail Date \_\_\_\_\_.
7.  Examiner's Amendment/Comment
8.  Examiner's Statement of Reasons for Allowance
9.  Other \_\_\_\_\_.

**DETAILED ACTION**

***Status of the Application***

Claims 1-6, 8-11, 29-36 are pending.

Amendment of claims 1-4, 6, 8-11, addition of claims 29-36, and cancellation of claim 7 in a communication filed on 12/15/2003 are acknowledged.

In a telephone conversation with Frank Mycroft on 3/26/2004, an agreement was reached to amend claims 1, 3, 8, 10-11, 30, 33 to place the application in condition for allowance. Applicant's representative requested a statement indicating that the authorized amendments to claims 1, 3, 8, 10-11, 30, 33 do not change the scope of the claims be of record.

***Information Disclosure Statement***

1. The information disclosure statement (IDS) submitted on 12/15/2003 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

***Examiner's Amendment***

2. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

3. Authorization for this Examiner's amendment was given in a telephone interview with Frank Mycroft on 3/26/2004:

4. Please replace claims 1, 3, 8, 10-11, 30 and 33 as follows:

1. A method of screening for a splicing defect in a human dihydropyrimidine dehydrogenase gene, wherein said gene comprises the sequence of SEQ ID NO: 1 or the variant thereof

wherein the residue at position 434 is an A and wherein said defect causes the exon of SEQ ID NO: 1 to be skipped, said method comprising determining whether said gene has an A residue or a G residue at said position 434, wherein the presence of an A residue, but not a G residue, at said position 434 indicates the presence of the splicing defect causing the exon of SEQ ID NO:1 to be skipped.

3. The method of claim 2, wherein the method comprises amplifying the fragment with a polymerase chain reaction primer from about 15 to about 20 nucleotides long, and wherein the nucleotide sequence of said primer is exactly complementary to a nucleotide sequence of SEQ ID NO: 1 between positions 434 and 861.

8. The method of claim 6, wherein the method comprises amplifying the genomic DNA with a polymerase chain reaction primer from about 15 to about 20 nucleotides long, and wherein the nucleotide sequence of said primer is exactly complementary to a nucleotide sequence of SEQ ID NO: 1 between positions 434 and 861.

10. A composition comprising a polymerase chain reaction primer from about 15 to about 20 nucleotides long wherein the nucleotide sequence of said primer is exactly complementary to a nucleotide sequence of SEQ ID NO: 1 between position 434 and position 861.

11. The composition of claim 10, wherein the nucleotide sequence of said primer is exactly complementary to a nucleotide sequence of SEQ ID NO: 1 between position 434 and position 534.

30. The method of claim 29, wherein the fragment of genomic DNA is amplified with a polymerase chain reaction primer from about 15 to about 20 nucleotides long, and wherein the nucleotide

sequence of said primer is exactly complementary to a nucleotide sequence of SEQ ID NO: 1 between positions 434 and 861.

33. A composition comprising a polymerase chain reaction primer from about 15 to about 20 nucleotides long, wherein the nucleotide sequence of said primer is exactly complementary to a nucleotide sequence of SEQ ID NO: 1 between position 1 and position 268.

***Reasons for Allowance***

5. The following is an Examiner's statement of reasons for allowance. Although the prior art discloses the cDNA encoding a human dihydropyrimidine dehydrogenase (Yokota et al., J. Biol. Chem. 269(37):23192-23196, 1994; cited in the IDS), the Examiner has found no teaching or suggestion in the prior art directed to the polynucleotide of SEQ ID NO: 1 or a method for detecting a splicing defect in a human dihydropyrimidine dehydrogenase gene comprising the nucleotide sequence of SEQ ID NO: 1, wherein a substitution at position 434 from G to A results in a splicing defect. The cDNA of Yokota et al. comprises nucleotides 267-293 and 295-433 of SEQ ID NO: 1. Therefore, claims 1-6, 8-9 and 29-36, directed to a method of screening for a splicing defect, a method of screening for 5-fluorouracil, or a method of testing a human for a single nucleotide polymorphism, wherein said methods comprise the step of detecting in genomic DNA comprising the polynucleotide of SEQ ID NO: 1, a substitution at position 434 of SEQ ID NO: 1, and claims 10-11, 33-35, directed to compositions comprising primers 15-20 nucleotides long which are completely complementary to nucleotides 1-268 or 434-861 of the polynucleotide of SEQ ID NO: 1, are allowable over the prior art of record.

6. Claims 1-6, 8-11 and 29-36 are allowed.

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7. Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
March 30, 2004

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PRIMARY EXAMINER  
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